

We Claim:

1. An isolated active fragment of an MEKK1 protein consisting of an amino acid sequence having at least 75% homology to an amino acid sequence consisting of about amino acids 875-1493 of Figure 9, wherein said active fragment mediates apoptosis.
2. The active fragment of claim 1, which consists of an amino acid sequence having at least 85% homology to an amino acid sequence consisting of about amino acids 875-1493 of Figure 9.
3. The active fragment of claim 1, which consists of an amino acid sequence having at least 95% homology to an amino acid sequence consisting of about amino acids 875-1493 of Figure 9.
4. The active fragment of claim 1, which is a mouse MEKK1 active fragment.
5. The active fragment of claim 1, which is a human MEKK1 active fragment.
6. The active fragment of claim 1, which is a rat MEKK1 active fragment.
7. The active fragment of claim 1, which consists of about amino acids 875-1493 of Figure 9.
8. A polypeptide comprising a kinase catalytic domain comprising a sequence selected from the group consisting of: amino acid residues from about 409 to about 672 of MEKK 1.1; amino acids from about 1331 to about 1594 of MEKK 1.2; a polypeptide at least 85% identical to amino acid residues 409 to about 672 of MEKK 1.1; and a polypeptide at least 85% identical to amino acid residues 1331 to about 1594 of MEKK 1.2.
9. An isolated protease-resistant MEKK1 protein comprising an amino acid sequence having at least 75% homology to the amino acid sequence of Figure 9, wherein at least one amino acid equivalent to amino acids 871-874 of Figure 9 is substituted such that the MEKK1 protein is resistant to proteolysis by a caspase after amino acid 874.
10. The MEKK1 protein of claim 9, wherein at least one amino acid equivalent to amino acids 871-874 of Figure 9 is substituted with an alanine residue.

11. The MEKK1 protein of claim 9, wherein each amino acid equivalent to amino acids 871-874 of Figure 9 is substituted with an alanine residue.

12. The MEKK1 protein of claim 9, which has at least 85% homology to the amino acid sequence of Figure 9.

13. The MEKK1 protein of claim 9, which has at least 95% homology to the amino acid sequence of Figure 9.

14. The MEKK1 protein of claim 9, which is a mouse MEKK1 protein.

15. The MEKK1 protein of claim 9, which is a human MEKK1 protein.

16. The MEKK1 protein of claim 9, which is a rat MEKK1 protein.

17. An isolated nucleic acid molecule consisting of a nucleotide sequence having at least 75% homology to a nucleotide sequence consisting of about nucleotides 645-2501 of SEQ ID NO:1, wherein said nucleic acid molecule encodes an active fragment of MEKK1 that mediates apoptosis.

18. The nucleic acid molecule of claim 17, which consists of a nucleotide sequence having at least 85% homology to a nucleotide sequence consisting of about nucleotides 645-2501 of SEQ ID NO:1.

19. The nucleic acid molecule of claim 17, which consists of a nucleotide sequence having at least 95% homology to a nucleotide sequence consisting of about nucleotides 645-2501 of SEQ ID NO:1.

20. The nucleic acid molecule of claim 17, which encodes an active fragment of a mouse MEKK1.

21. The nucleic acid molecule of claim 17, which encodes an active fragment of a human MEKK1.

22. The nucleic acid molecule of claim 17, which encodes an active fragment of a rat MEKK1.

23. The nucleic acid molecule of claim 17, which consists of about nucleotides 645-2501 of SEQ ID NO:1, or a nucleotide sequence that, due to the degeneracy of the genetic code, encodes the same amino acid sequence as about nucleotides 645-2501 of SEQ ID NO:1.

24. The nucleic acid molecule of claim 17, which consists of nucleotides 645-2501 of SEQ ID NO:1, or a nucleotide sequence that, due to the degeneracy of the genetic code, encodes the same amino acid sequence as nucleotides 645-2501 of SEQ ID NO:1.

25. An isolated nucleic acid molecule encoding a protease-resistant MEKK1 protein, wherein the protease resistant MEKK1 protein comprises an amino acid sequence having at least 75% homology to the amino acid sequence of Figure 9 and at least one codon of the nucleic acid molecule encoding an amino acid equivalent to at least one of amino acids 871-874 of Figure 9 is mutated such the encoded MEKK1 protein is resistant to proteolysis by a caspase after an amino acid equivalent to amino acid 874 of Figure 9.

26. The nucleic acid molecule of claim 25, wherein the MEKK1 protein comprises an amino acid sequence having at least 85% homology to the amino acid sequence of Figure 9.

27. The nucleic acid molecule of claim 25, wherein the MEKK1 protein comprises an amino acid sequence having at least 95% homology to the amino acid sequence of Figure 9.

28. The nucleic acid molecule of claim 25, which encodes a protease-resistant mouse MEKK1 protein.

29. The nucleic acid molecule of claim 25, which encodes a protease-resistant human MEKK1 protein.

30. The nucleic acid molecule of claim 25, which encodes a protease-resistant rat MEKK1 protein.

31. An expression vector comprising the nucleic acid molecule of claim 17.

32. An expression vector comprising the nucleic acid molecule of claim 25.

33. A host cell containing the expression vector of claim 31.
34. A host cell containing the expression vector of claim 32.
35. A method of stimulating apoptosis in a cell comprising introducing into the cell an expression vector encoding the MEKK1 active fragment of claim 1 such that MEKK1 active fragment is produced in the cell and apoptosis is stimulated.
36. A method of inhibiting apoptosis in a cell comprising introducing into the cell an expression vector encoding the protease-resistant MEKK1 protein of claim 9 such that protease-resistant MEKK1 protein is produced in the cell and apoptosis is inhibited.
37. A method of generating an MEKK1 active fragment *in vitro*, comprising:
contacting an MEKK1 protein *in vitro* with a caspase protease under proteolysis conditions; and
allowing the caspase protease to cleave the MEKK1 protein such that an MEKK1 active fragment is generated.
38. A method of identifying a compound that modulates the apoptotic activity of an MEKK1 active fragment, comprising:
providing an indicator cell that comprises the MEKK1 active fragment of claim 1;
contacting the indicator cell with a test compound; and
determining the effect of the test compound on the apoptotic activity of the MEKK1 active fragment in the indicator cell to thereby identify a compound that modulates the apoptotic activity of the MEKK1 active fragment.
39. A human MEKK1 polypeptide that is at least 80% identical to the sequence set forth in figure 9.
40. A human MEKK1 polypeptide that is 80% identical to the sequence set forth in Figure 9, wherein said polypeptide has a kinase activity.